

**REMARKS**

Claims 2-5, 8-31 and 34-37 are pending in the present application. By virtue of this response, claims 10, 21, 23, and 29 have been amended; no claims are added or cancelled in this response. Claims 1, 6, 7, 32 and 33 were cancelled in a previous response. Accordingly, claims 2-5, 8-31 and 34-37 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any of the subject matter of the claims as previously presented.

Claim 10 is amended to correct a typographical error. Amendments to claims 21, 23, and 29 are discussed below.

***Prior Claim Objections/Rejections***

Applicants thank the Examiner for indicating that the prior objection to claims 2, 21 and 23 have been overcome by the amendment filed October 13, 2006; for indicating that the prior rejection of Claims 1-5 and 8-31 under 35 U.S.C. § 112, first paragraph, has been overcome by cancellation of claim 1 and by deletion of the recitation, "wherein the tin mesoporphyrin is not derivatized with a complexing agent" in claims 5 and 11; for indicating that the prior rejection of Claims 1-5 and 8-31 under 35 U.S.C. § 112, second paragraph, has been overcome by cancellation of claim 1 and amendments to claims 23 and 26; and for indicating that the rejection of Claims 22 and 30 under 35 U.S.C. § 102(b) as being anticipated by Kappas et al (US 4,692,440) has been overcome by the amendment filed October 13, 2006.

***New Rejection Under 35 U.S.C. § 112, Second Paragraph***

Claims 21, 23-28 and 31 stand rejected under 35 USC § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In response, Applicants have amended claims 21 and 23 to clarify that the product of the hemin hydrogenation is a mesoporphyrin formate, which is then subjected to a tin insertion step. Applicants submit that this amendment renders claims 21, 23, and their dependent claims 24-28 and 31 definite, and respectfully request withdrawal of the rejection.



themselves contain multiple possibilities—e.g., “substituted or unsubstituted alkyl” certainly represents considerably more than one choice—which causes the numbers to become even more astronomical. A genus that has over ten million googol possible compounds cannot be said to “teach” tin mesoporphyrin complexed with amino acids.<sup>1</sup>

The Examiner stated that “Robinson teaches that one of the preferred metal ions complexed to the core is Tin (page 32, paragraph 183) and the compounds of Robinson are complexed to amino acids.” The cited section of Robinson states:

For the use of the agents according to the invention for photodynamic therapy, the porphyrin or azaporphyrin compound should be metal free, i.e., M=2H, or should have coordinated photoactive metals, preferred examples of which include zinc, indium, gallium, tin, germanium, palladium, platinum, aluminum, silicon, ruthenium, yttrium, ytterbium, magnesium, lutetium, and cadmium. (US 2003/0100752 paragraph 183, emphasis added.)

Robinson mentions fifteen metals in this list, and also includes the metal-free porphyrin as an option. More importantly, Robinson does not specify which of the compounds in his disclosure (as noted, the genus of claim 1 discloses over  $10^{107}$  compounds) is meant by “the agents” which are to be chosen to bear one of these fifteen metals (or which should be metal-free, a sixteenth possibility).

The secondary reference by Drummond does not even mention mesoporphyrin or amino acids. It discusses a variety of protoporphyrin compounds with a variety of metals. While tin protoporphyrin was the most potent compound *in vitro*, the most potent compound *in vivo* was chromium protoporphyrin, which reduced rat liver heme oxygenase activity to  $0.29 \pm 0.04$  nmol bilirubin/mg/hr; corresponding numbers for manganese protoporphyrin and tin protoporphyrin were  $1.05 \pm 0.16$  and  $1.08 \pm 0.13$ , respectively (see Table 2 at page 89). Given that a combination of references must between them teach all the limitations of the claims, Drummond cannot make up

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<sup>1</sup> The only location where Robinson even mentions mesoporphyrin appears to be at Table 1 at page 19; the distinct compounds “aza-mesoporphyrin” and “aza-isomesoporphyrin” are mentioned in Table 2 at page 23. This was determined by searching for the word “mesoporphyrin” in the USPTO text record for US 2003/0100752 available at <http://appft1.uspto.gov/netathtml/PTO/srchnum.html>.

for the deficiency of the Robinson reference in arriving at the invention as instantly claimed. The Bettelheim et al (General, Organic, and Biochemistry, 1998, page 596), discussing the zwitterionic properties of amino acids, does not remedy the deficiency in the Robinson reference.

The Robinson reference combined with the Drummond and Bettelheim references cannot support a *prima facie* case of obviousness. Accordingly, Applicants respectfully request withdrawal of the rejection of claims 2-5, 8-10, 22, 29-30 and 34-37.

With respect to Niedballa et al (US 5,275,801), the cited patent does not even teach mesoporphyrin, let alone tin mesoporphyrin, and thus does not disclose all the elements of the instant claims. No secondary reference is provided to remedy this deficiency.

The Examiner makes conclusory statements that it “would have been obvious to one of ordinary skill in the art at the time the invention was made to mesoporphyrins [*sic*] as instantly claimed by making insignificant changes to the method taught in the prior art. One of ordinary skill in the art would have been motivated to do so since the method of Niedballa is a general method applicable to the porphyrin core and gives high yields.” (Office Action mailed April 14, 2006, page 9, third paragraph.) Similar statements are made in the last Office Action: “The method of Niedballa is a general one and can be applied to the porphyrin core. The yields are also high. Hence there is motivation to sue [*sic*, use] the method of Niedballa.” (Office Action mailed January 11, 2007, page 7, paragraph immediately preceding the heading “Conclusion.”) However, no reasoning is presented as to why one would alter the structure of Niedballa’s compounds to arrive at the Applicants’ specific invention. Indeed, if Niedballa’s goal is to arrive at a more water-soluble porphyrin, altering the Niedballa compounds to the structure of a mesoporphyrin would make them less water soluble. Since Niedballa does not teach all the limitations of the instant claims, and no reason for modifying Niedballa to arrive at the limitations of the instant claims is provided, a *prima facie* case of obviousness has not been presented.

Accordingly, Applicants respectfully request the withdrawal of this rejection of claims 11-20.

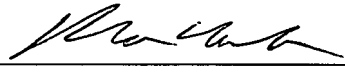
**CONCLUSION**

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 606952000500. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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